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Docket No. 48231-A-PCT-US/JPW/ASM/MML

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Iva Greenwald and Diane Levitan

Serial No. : 09/043,944

Filed : March 27, 1998

For : IDENTIFICATION OF SEL-12 AND USES THEREOF

1185 Avenue of the Americas
New York, New York 10036
June 21, 2002

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following references which are listed on the PTO-1449 form attached hereto as **Exhibit A**. Copies of these references are submitted herewith as **Exhibits 1-22**, respectively.

1. U.S. Patent No. 5,840,540, issued November 24, 1998, Peter H. St. George-Hyslop et al. (**Exhibit 1**);
2. U.S. Patent No. 6,087,153, issued July 11, 2000, Greenwald et al. (**Exhibit 2**);
3. U.S. Patent No. 6,376,239, issued April 23, 2002, Baumeister (**Exhibit 3**);

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4. Daigle I., and Li C., "apl-1, a *Caenorhabditis elegans* gene encoding a protein related to the human beta-amyloid protein precursor" *Proc. Natl. Acad. Sci. U.S.A.* (1993) 90(24):12045-9 (**Exhibit 4**);
5. Database dbEST, National Center for Biotechnology Information, National Library of Medicine, GenBank Accession No. H19012 (1995) (**Exhibit 5**);
6. Database EMBL Accession No: U35660 (1995) Levitan D., Greenwald I., "Caenorhabditis elegans membrane protein (sel-12) mRNA" XP002176178 (**Exhibit 6**);
7. Fire A., et al., "A modular set of lacZ fusion vectors for studying gene expression in *Caenorhabditis elegans*" *Gene* (1990) 93(2):189-98 (**Exhibit 7**);
8. Fitzgerald K., and Greenwald I., "Interchangeability of *Caenorhabditis elegans* DSL proteins and intrinsic signalling activity of their extracellular domains in vivo" *Development* (1995) 121(12):4275-82 (**Exhibit 8**);
9. Greenwald I., "Structure/function studies of lin-12/Notch proteins" *Curr. Opin. Genet. Dev.* (1994) 4(4):556-62 (**Exhibit 9**);
10. Hedgecock E. M. and Herman R. K., "The ncl-1 gene and genetic mosaics of *Caenorhabditis elegans*" *Genetics* (1995) 141(3):989-1006 (**Exhibit 10**);
11. Hedgecock E. M., et al., "Genetics of cell and axon migrations in *Caenorhabditis elegans*" *Development* (1987) 100(3):365-82 (**Exhibit 11**);

12. Levitan D. and Greenwald I., "Facilitation of lin-12-mediated signalling by sel-12, a *Caenorhabditis elegans* S182 Alzheimer's disease gene" *Nature* (1995) 377(6547): 351-4 (**Exhibit 12**);
13. Levy-Lahad E., et al., "Genomic structure and expression of STM2, the chromosome 1 familial Alzheimer disease gene" *Genomics* (1996) 34(2):198-204 (**Exhibit 13**);
14. Li X. and Greenwald I., "HOP-1, a *Caenorhabditis elegans* presenilin, appears to be functionally redundant with SEL-12 presenilin and to facilitate LIN-12 and GLP-1 signaling" *Proc. Natl. Acad. Sci. U.S.A.* (1997) 94(22):12204-9 (**Exhibit 14**);
15. Rogaev E. I., et al., "Familial Alzheimer's disease in kindreds with missense mutations in a gene on chromosome 1 related to the Alzheimer's disease type 3 gene" *Nature* (1995) 376(6543):775-8 (**Exhibit 15**);
16. Sherrington R., et al., "Cloning of a gene bearing missense mutations in early-onset familial Alzheimer's disease" *Nature* (1995) 375(6534):754-60 (**Exhibit 16**);
17. Stratagene Cloning Systems Catalog, 1993, pages 27, 31, 32, and 313 (**Exhibit 17**);
18. Sundaram M. and Greenwald I., "Genetic and phenotypic studies of hypomorphic lin-12 mutants in *Caenorhabditis elegans*" *Genetics* (1993) 135(3):755-63 (**Exhibit 18**);

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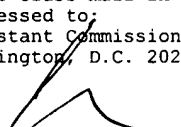
19. Sundaram M. and Greenwald I., "Suppressors of a lin-12 hypomorph define genes that interact with both lin-12 and glp-1 in *Caenorhabditis elegans*" *Genetics* (1993) 135(3):765-83 (**Exhibit 19**);
20. Wen C., et al., "spr-2, a suppressor of the egg-laying defect caused by loss of sel-12 presenilin in *Caenorhabditis elegans*, is a member of the SET protein subfamily" *Proc. Natl. Acad. Sci. U.S.A.* (2000) 97(26):14524-9 (**Exhibit 20**);
21. Wilkinson H. A. and Greenwald I., "Spatial and temporal patterns of lin-12 expression during *C. elegans* hermaphrodite development" *Genetics* (1995) 141(2):513-26 (**Exhibit 21**); and
22. Wilkinson H. A., et al., "Reciprocal changes in expression of the receptor lin-12 and its ligand lag-2 prior to commitment in a *C. elegans* cell fate decision" *Cell* (1994) 79(7):1187-98 (**Exhibit 22**).

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No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.	
 Alan J. Morrison Reg. No. 37,399	<u>6/21/02</u> Date

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